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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/665,976	09/20/2000	Lawrence W. Stanton	SCIOS.014A	8472

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EXAMINER	
SOUAYA, JEHANNE E	
ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 04/08/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/665,976	STANTON ET AL.	
	Examiner	Art Unit	
	Jehanne E Souaya	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 January 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Claim 31 is pending in the instant application. Claims 1-7, 30, 32, and 33 have been canceled. Claim 31 was indicated as allowable in the previous office action, however, upon reconsideration of the claim, a new issue has been raised with regard to 35 USC 101 and 35 USC 112/first paragraph. The following office action contains new grounds for rejection, and therefore, finality of the rejection of the last Office action is withdrawn. This action is NON-FINAL.

Claim Rejections - 35 USC § 101

2. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

3. Claim 31 is rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility.

Definitions: [from REVISED INTERIM UTILITY GUIDELINES TRAINING MATERIALS; repeated from http://www.uspto.gov/web/menu/utility.pdf]
"Credible Utility" - Where an applicant has specifically asserted that an invention has a particular utility, that assertion cannot simply be dismissed by Office personnel as being "wrong". Rather, Office personnel must determine if the assertion of utility is credible (i.e., whether the assertion of utility is believable to a person of ordinary skill in the art based on the totality of evidence and reasoning provided). An assertion is credible unless (A) the logic underlying the assertion is seriously flawed, or (B) the facts upon which the assertion is based is inconsistent with the logic underlying the assertion. Credibility as used in this context refers to the reliability of the statement based on the logic and facts that are offered by the applicant to support the assertion of utility. A credible utility is assessed from the standpoint of whether a person of ordinary skill in the art would accept that the recited or disclosed invention is currently available for such use. For example, no perpetual motion machines would be considered to be currently available. However, nucleic acids could be used as probes, chromosome markers, or forensic or diagnostic markers. Therefore, the credibility of such an assertion would not be questioned, although such a use might fail the specific and substantial tests (see below).

"Specific Utility" - A utility that is specific to the subject matter claimed. This contrasts with a general utility that would be applicable to the broad class of the invention. For example, a claim to a polynucleotide whose use is disclosed simply as a "gene probe" or "chromosome marker" would not be considered to be specific in the absence of a disclosure of a specific DNA target. Similarly, a general statement of diagnostic utility, such as diagnosing an unspecified disease, would ordinarily be insufficient absent a disclosure of what condition can be diagnosed.

"Substantial utility" - A utility that defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities. For example, both a therapeutic method of treating a known or newly discovered disease and an assay method for identifying compounds that themselves have a "substantial utility" define a "real world" context of use. An assay that measures the presence of a material which has a stated correlation to a predisposition to the onset of a particular disease condition would also define a "real world" context of use in identifying potential candidates for preventive measures or further monitoring. On the other hand, the following are examples of situations that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use and, therefore, do not define "substantial utilities":

A. Basic research such as studying the properties of the claimed product itself or the mechanisms in which the material is involved.

B. A method of treating an unspecified disease or condition. (Note, this is in contrast to the general rule that treatments of specific diseases or conditions meet the criteria of 35 U.S.C. ' 101.)

C. A Method of assaying for or identifying a material that itself has no "specific and/or substantial utility."

D. A method of making a material that itself has no specific, substantial, and credible utility.

E. A claim to an intermediate product for use in making a final product that has no specific, substantial, and credible utility.

Note that "throw away" utilities do not meet the tests for a specific or substantial utility. For example, using transgenic mice as snake food is a utility that is neither specific (all mice could function as snake food) nor substantial (using a mouse costing tens of thousands of dollars to produce as snake food is not a "real world" context of use). Similarly, use of any protein as an animal food supplement or a shampoo ingredient are "throw away" utilities that would not pass muster as specific or substantial utilities under 35 U.S.C. ' 101. This analysis should, or course, be tempered by consideration of the context and nature of the invention. For example, it a transgenic mouse was generated with the specific provision of an enhanced nutrient profile, and disclosed for use as an animal food, then the test for specific and substantial asserted utility would be considered to be met.

A "Well established utility" - a specific, substantial, and credible utility which is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material, alone or taken with the knowledge of one skilled in the art. "Well established utility" does not encompass any "throw away" utility that one can dream up for an invention or a nonspecific utility that would apply to virtually every member of a general class of materials, such as proteins or DNA. If this is the case, any product or apparatus, including perpetual motion machines, would have a "well established utility" as landfill, an amusement device, a toy, or a paper weight; any carbon containing molecule would have a "well established utility" as a fuel since it can be burned; any protein would have well established utility as a protein supplement for animal food. This is not the intention of the statute.
See also the MPEP at 2107 - 2107.02.

The claimed nucleic acids are not supported by a specific asserted utility because the disclosed uses of the nucleic acids are not specific and are generally applicable to any nucleic acid. The specification teaches that the invention is based on the identification of a gene that is differentially expressed in the left ventricle of the rat Myocardial infarction model, in the rat Cardiac Hypertrophy Model, and in the mouse Viral Myocarditis model (p. 20, lines 9-11). Claim 31 is directed to the cDNA sequence of that gene. The specification states that the nucleic

acids of the invention, and particularly SEQ ID NO 2 can be used to design specific probes and primers, can be used in detection, diagnostic, prognostic methods, vector constructs, antibody constructs, etc (p. 42-48). These are non-specific uses that are applicable to nucleic acids in general and not particular or specific to the nucleic acid being claimed.

Further, the claimed nucleic acids are not supported by a substantial utility because no substantial utility has been established for the claimed subject matter. The specification states that when characterization of the differentially expressed genes indicate that modulation of the gene's expression or the gene product's activity can inhibit or treat a disease, specifically cardiac, kidney, or inflammatory diseases, the differentially expressed gene or it's gene product becomes a potential drug candidate or a target for developing a drug candidate for the treatment of a cardiac, kidney or inflammatory disease, or may be used as a diagnostic. However, the specification has not taught the activity of the polypeptide encoded by SEQ ID NO 2, nor has the specification demonstrated that the modulation of the expression of SEQ ID NO 2 can be used to inhibit or treat any kidney, inflammatory, or cardiac disease, including viral myocarditis, cardiac hypertrophy, or myocardial infarction. The need for such research clearly indicates that the nucleic acid or the protein it encodes is not disclosed as to a currently available or substantial utility. A starting material that can only be used to produce a final product does not have substantial asserted utility in those instances where the final product is not supported by a specific and substantial utility. Further, a starting material does not have substantial utility when further experimentation must be conducted to determine the use for that starting material. The research contemplated by applicant(s) to characterize potential protein products, and determine therapeutic and diagnostic uses does not constitute a specific and substantial utility. Identifying

and studying the properties of a nucleic acid or protein itself or the mechanisms in which such are involved does not define a "real world" context or use. Similarly, the other listed and asserted utilities as summarized above or in the instant specification are neither substantial nor specific due to being generic in nature and applicable to a myriad of such compounds. Note, because the claimed invention is not supported by a specific and substantial asserted utility for the reasons set forth above, credibility of the utility has not been assessed. Neither the specification as filed nor any art of record discloses or suggests any property or activity for the nucleic acid and/or protein compound(s) such that another non-asserted utility would be well established for the compounds.

It is noted that the specification asserts that the differentially expressed nucleic acids can be used as a diagnostic. This assertion has been thoroughly reviewed, however the teachings of the specification do not support how one of skill in the art would use the claimed nucleic acid as a diagnostic. Firstly, it is noted that the specification teaches that in vivo experimentation revealed that in the rat myocardial infarction model and the rat cardiac hypertrophy model, the gene corresponding to SEQ ID NO 2 was under expressed by about 1.8 fold and 2.5 fold, respectively. This expression pattern, however, does not appear to be diagnostic of cardiac diseases in general as the specification teaches that in vivo, the gene corresponding to SEQ ID NO 2 was over expressed in the mouse viral myocarditis model (See p. 65, lines 15-24). Furthermore, the specification fails to teach corroborative evidence for such *in vivo* expression patterns. The specification teaches that in *in vitro* experiments, rat cardiac myocytes were treated with various growth factors and cytokines known to induce cardiac hypertrophy (see p. 72, lines 7-9). However, while SEQ ID NO 2 was under expressed in the in vivo rat cardiac hypertrophy model, it was over expressed in cardiac myocytes cells where cardiac hypertrophy was induced (see p.

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74, and figure 4). Therefore, given the results in the specification, the skilled artisan would not be able to identify a specific cardiac disease based on detection of either over expression or under expression of SEQ ID NO 2. Further experimentation would be required of the skilled artisan to reasonably confirm a real world context of use for the claimed nucleic acids.

Claim Rejections - 35 USC § 112

Claim 31 is also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

The claim is drawn to an isolated nucleic acid comprising the sequence of SEQ ID NO 2, or the portion of SEQ ID NO 2 that codes SEQ ID NO 1.

While the specification asserts that the differentially expressed nucleic acids can be used as a diagnostic. This assertion has been thoroughly reviewed, however the teachings of the specification do not support how one of skill in the art would use the claimed nucleic acid as a diagnostic. Firstly, it is noted that the specification teaches that in vivo experimentation revealed that in the rat myocardial infarction model and the rat cardiac hypertrophy model, the gene corresponding to SEQ ID NO 2 was under expressed by about 1.8 fold and 2.5 fold, respectively. This expression pattern, however, does not appear to be diagnostic of cardiac diseases in general as the specification teaches that in vivo, the gene corresponding to SEQ ID NO 2 was over expressed in the mouse viral myocarditis model (See p. 65, lines 15-24). Furthermore, the

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specification fails to teach corroborative evidence for such *in vivo* expression patterns. The specification teaches that in *in vitro* experiments, rat cardiac myocytes were treated with various growth factors and cytokines known to induce cardiac hypertrophy (see p. 72, lines 7-9). However, while SEQ ID NO 2 was under expressed in the in vivo rat cardiac hypertrophy model, it was over expressed in cardiac myocytes cells where cardiac hypertrophy was induced (see p. 74, and figure 4). The specification provides no guidance as to the differences in expression pattern of SEQ ID NO 2 with regard to these cardiac diseases. Therefore, given the results in the specification, the skilled artisan would not be able to identify a specific cardiac disease based on detection of either over expression or under expression of SEQ ID NO 2. Further empirical experimentation would be required for the skilled artisan to determine a use for the claimed nucleic acid. This experimentation would largely consist of trial and error analysis, as the results in the specification demonstrate the unpredictability of the use for SEQ ID NO 2 as a diagnostic. The art does not provide any teaching to overcome the unpredictability taught in the specification. Therefore, the experimentation required of the skilled artisan to determine how to use the claimed nucleic acid is considered undue.

Conclusion

4. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Souaya whose telephone number is (703) 308-6565. The examiner can normally be reached Monday-Friday from 9:00 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for this Group is (703) 305-3014.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Jehanne Souaya

Jehanne Souaya
Patent examiner
Art Unit 1634
4/3/03